

WHAT IS CLAIMED IS:

1. A method for diagnosing glaucoma in a patient which comprises the steps:
  - (A) incubating under conditions permitting nucleic acid hybridization: a marker nucleic acid molecule, said first marker nucleic acid molecule comprising a nucleotide sequence of a polynucleotide that specifically hybridizes to a polynucleotide that is linked to a TIGR promoter, and a complementary nucleic acid molecule obtained from a cell or a bodily fluid of said patient, wherein nucleic acid hybridization between said marker nucleic acid molecule, and said complementary nucleic acid molecule obtained from said patient permits the detection of a polymorphism whose presence is predictive of a mutation affecting TIGR response in said patient;
  - (B) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient; and
  - (C) detecting the presence of said polymorphism, wherein the detection of said polymorphism is diagnostic of glaucoma.
2. A method for diagnosing glaucoma in a patient according to claim 1, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt1*.
3. A method for diagnosing glaucoma in a patient according to claim 1, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt2*.
4. A method for diagnosing glaucoma in a patient according to claim 1, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt3*.
5. A method for diagnosing glaucoma in a patient according to claim 1, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt4*.
6. A method for diagnosing glaucoma in a patient according to claim 1, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt5*.
7. A method for diagnosing glaucoma in a patient according to claim 1, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRsv1*.
8. A method for diagnosing glaucoma in a patient according to claim 1, further comprising a second marker nucleic acid molecule.
9. A method for diagnosing glaucoma in a patient according to claim 8, wherein said first marker nucleic acid molecule and said second marker nucleic acid molecule are selected from the group consisting of a nucleic acid molecule that comprises the sequence of SEQ ID NO: 6, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 7, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 8, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 9, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 10, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 11, a nucleic acid molecule that

comprises the sequence of SEQ ID NO: 12, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 13, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 14, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 15, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 16, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 17, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 18, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 19, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 20, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 21, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 22, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 23, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 24 and a nucleic acid molecule that comprises the sequence of SEQ ID NO: 25.

10. A method for diagnosing glaucoma in a patient according to claim 9, wherein said first marker nucleic acid molecule and said second marker nucleic acid molecule are selected from the group consisting of a nucleic acid molecule that comprises the sequence of SEQ ID NO: 6, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 7, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 8, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 9, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 12, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 13, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 18, and a nucleic acid molecule that comprises the sequence of SEQ ID NO: 25

11. A method for diagnosing glaucoma in a patient according to claim 10, wherein said first marker nucleic acid molecule is a nucleic acid molecule that comprises the sequence of SEQ ID NO: 13 and said second marker nucleic acid molecule is a nucleic acid molecule that comprises the sequence of SEQ ID NO: 12.

12. A method for diagnosing glaucoma in a patient according to claim 10, wherein said first marker nucleic acid molecule is a nucleic acid molecule that comprises the sequence of SEQ ID NO: 9 and said second marker nucleic acid molecule is a nucleic acid molecule that comprises the sequence of SEQ ID NO: 8.

13. A method for diagnosing glaucoma in a patient according to claim 10, wherein said first marker nucleic acid molecule is a nucleic acid molecule that comprises the sequence of SEQ ID NO: 7 and said second marker nucleic acid molecule is a nucleic acid molecule that comprises the sequence of SEQ ID NO: 6.

14. A method for diagnosing glaucoma in a patient according to claim 10, wherein said first marker nucleic acid molecule is a nucleic acid molecule that comprises the sequence of SEQ ID NO: 18 and said second marker nucleic acid molecule is a nucleic acid molecule that comprises the sequence of SEQ ID NO: 25.

15. A method for diagnosing steroid sensitivity in a patient which comprises the steps:
- (A) incubating under conditions permitting nucleic acid hybridization: a marker nucleic acid molecule, said marker nucleic acid molecule comprising a nucleotide sequence of a polynucleotide that is linked to a TIGR promoter, and a complementary nucleic acid molecule obtained from a cell or a bodily fluid of said patient, wherein nucleic acid hybridization between said marker nucleic acid molecule, and said complementary nucleic acid molecule obtained from said patient permits the detection of a polymorphism whose presence is predictive of a mutation affecting TIGR response in said patient;
  - (B) permitting hybridization between said TIGR-encoding marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient; and
  - (C) detecting the presence of said polymorphism, wherein the detection of said polymorphism is diagnostic of steroid sensitivity.
16. A method for diagnosing steroid sensitivity in a patient according to claim 15, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt1*.
17. A method for diagnosing steroid sensitivity in a patient according to claim 15, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt2*.
18. A method for diagnosing steroid sensitivity in a patient according to claim 15, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt3*.
19. A method for diagnosing steroid sensitivity in a patient according to claim 15, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt4*.
20. A method for diagnosing steroid sensitivity in a patient according to claim 15, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt5*.
21. A method for diagnosing steroid sensitivity in a patient according to claim 15, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRsv1*.
22. A method for diagnosing steroid sensitivity in a patient according to claim 15, further comprising a second marker nucleic acid molecule.
23. A method for diagnosing steroid sensitivity in a patient according to claim 22, wherein said first marker nucleic acid molecule and said second marker nucleic acid molecule are selected from the group consisting of a nucleic acid molecule that comprises the sequence of SEQ ID NO: 6, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 7, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 8, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 9, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 10, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 11, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 12, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 13, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 14, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 15, a nucleic acid



30. The method of claim 1, wherein said marker nucleic acid molecule is selected from the group consisting of D1S2536 marker nucleic acid, D1S210 marker nucleic acid, D1S1552 marker nucleic acid, D1S2536 marker nucleic acid D1S2790 marker nucleic acid, SHGC-12820 marker nucleic acid, and D1S2558 marker nucleic acid.

32. The method of claim 15, wherein said marker nucleic acid molecule is selected from the group consisting of D1S2536 marker nucleic acid, D1S210 marker nucleic acid, D1S1552 marker nucleic acid, D1S2536 marker nucleic acid D1S2790 marker nucleic acid, SHGC-12820 marker nucleic acid, and D1S2558 marker nucleic acid.

34. A nucleic acid molecule that comprises the sequence of SEQ ID NO: 1.

36. A substantially purified molecule that specifically binds to a nucleic acid molecule that comprises the sequence of SEQ ID NO:1.

37. A nucleic acid molecule that comprises the sequence of SEQ ID NO: 3.

38. A recombinant DNA molecule containing a polynucleotide that specifically hybridizes to  
SEQ ID NO: 3.

39. A substantially purified molecule that specifically binds to a nucleic acid molecule that comprises the sequence of SEQ ID NO: 3.

40. A nucleic acid molecule that comprises the sequence of SEQ ID NO: 4.

41. A recombinant DNA molecule containing a polynucleotide that specifically hybridizes to  
SEQ ID NO: 4.

42. A substantially purified molecule that specifically binds to a nucleic acid molecule that comprises the sequence of SEQ ID NO: 4.

43. A nucleic acid molecule that comprises the sequence of SEQ ID NO: 5.

44. A recombinant DNA molecule containing a polynucleotide that specifically hybridizes to  
SEQ ID NO: 5.

45. A substantially purified molecule that specifically binds to a nucleic acid molecule that comprises the sequence of SEQ ID NO: 5.

46. A nucleic acid molecule that comprises the sequence of SEQ ID NO: 26.

47. A recombinant DNA molecule containing a polynucleotide that specifically hybridizes to  
SEQ ID NO: 26.

48. A substantially purified molecule that specifically binds to a nucleic acid molecule that comprises the sequence of SEQ ID NO: 26.

49. A substantially purified molecule that specifically binds to a nucleic acid molecule selected from the group consisting of a nucleic acid molecule that comprises a *cis* element characteristic of PRL-FP111, a nucleic acid molecule that comprises a glucocorticoid response *cis* element, a nucleic acid molecule that comprises a *cis* element characteristic of GR/PR, a nucleic acid molecule that comprises a shear stress response *cis* element, a nucleic acid molecule that comprises a glucocorticoid response *cis* element, a nucleic acid molecule that comprises a *cis* element characteristic of CBE, a nucleic acid molecule that comprises a *cis* element capable of binding NFE, a nucleic acid molecule that comprises a *cis* element capable of binding KTF.1-CS, a nucleic acid molecule that comprises a *cis* element characteristic of PRE, a nucleic acid molecule that comprises a *cis* element characteristic of ETF-EGFR, a nucleic acid molecule that comprises a *cis* element capable of binding SRE-cFos, a nucleic acid molecule that comprises a *cis* element characteristic of Alu, a nucleic acid molecule that comprises a *cis* element capable of binding VBP, a nucleic acid molecule that comprises a *cis* element characteristic of Malt-CS, a nucleic acid molecule that comprises a *cis* element capable of binding ERE, a nucleic acid molecule that comprises a *cis* element characteristic of NF-mutagen, a nucleic acid molecule that comprises a *cis* element capable of binding myc/PRF, a nucleic acid molecule that comprises a *cis* element capable of binding AP2, a nucleic acid molecule that comprises a *cis* element capable of binding HSTF, a nucleic acid molecule that comprises a *cis* element characteristic of SBF, a nucleic acid molecule that comprises a *cis* element capable of binding NF-1, a nucleic acid molecule that comprises a *cis* element capable of binding NF-MHCIIA/B, a nucleic acid molecule that comprises a *cis* element capable of binding PEA1, a nucleic acid molecule that comprises a *cis* element characteristic of ICS, a nucleic acid molecule that comprises a *cis* element capable of binding ISGF2, a nucleic acid molecule that comprises a *cis* element capable of binding zinc, a nucleic acid molecule that comprises a *cis* element characteristic of CAP/CRP-galO, a nucleic acid molecule that comprises a *cis* element capable of binding AP1, a nucleic acid molecule that comprises a *cis* element capable of binding SRY, a nucleic acid molecule that comprises a *cis* element characteristic of GC2, a nucleic acid molecule that comprises a *cis* element capable of binding PEA3, a nucleic acid molecule that comprises a *cis* element characteristic of MIR, a nucleic acid molecule that comprises a *cis* element capable of binding NF-HNF-1, a nucleic acid molecule that comprises a thyroid receptor *cis* element, and a nucleic acid molecule that comprises a *cis* element capable of binding NFκB.

50. A method of treating glaucoma which comprises administering to a glaucomatous patient an effective amount of an agent capable of binding a cis element located within SEQ ID NO: 1.

51. The method of claim 50, wherein said agent inhibits the expression of a TIGR mRNA.



wherein nucleic acid hybridization between said marker nucleic acid molecule, and said complementary nucleic acid molecule obtained from said patient permits the detection of a polymorphism whose presence is predictive of a mutation affecting TIGR response in said patient;

(B) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said patient; and

(C) detecting the presence of said polymorphism, wherein the detection of said polymorphism is prognostic of glaucoma.

55. A method for prognosing glaucoma in a patient according to claim 54, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt1*.

56. A method for prognosing glaucoma in a patient according to claim 54, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt2*.

57. A method for prognosing glaucoma in a patient according to claim 54, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt3*.

58. A method for prognosing glaucoma in a patient according to claim 54, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt4*.

59. A method for prognosing glaucoma in a patient according to claim 54, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRmt5*.

60. A method for prognosing glaucoma in a patient according to claim 54, wherein said marker nucleic acid molecule is capable of specifically detecting *TIGRsv1*.

61. A method for prognosing glaucoma in a patient according to claim 54, further comprising a second marker nucleic acid molecule.

62. A method for prognosing glaucoma in a patient according to claim 61, wherein said first marker nucleic acid molecule and said second marker nucleic acid molecule are selected from the group consisting of a nucleic acid molecule that comprises the sequence of SEQ ID NO: 6, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 7, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 8, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 9, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 10, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 11, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 12, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 13, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 14, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 15, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 16, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 17, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 18, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 19, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 20, a nucleic acid molecule that comprises the sequence of SEQ ID NO: 21, a nucleic acid molecule that comprises the sequence of SEQ ID





specifically hybridizes to a nucleic acid possessing the characteristic C to T substitution of the mt11 sequence variant, and a region of SEQ ID NO: 33 or its complement that specifically hybridizes to a nucleic acid possessing the characteristic C to T substitution of the TIGRmt11 sequence variant but does not specifically hybridize to a nucleic acid that does not possess the TIGRmt11 sequence variant under high stringency conditions.

71. A nucleic acid that specifically hybridizes to the nucleic acid of claim 70.
72. A vector comprising the nucleic acid of claim 70.
73. A cell comprising the nucleic acid of claim 70.
74. A method for detecting the presence or absence of the characteristic TIGRmt11 sequence variation in a sample containing DNA, comprising contacting a labeled nucleic acid of claim 70 with the DNA of the sample under hybridization conditions and determining the presence of hybrid nucleic acid molecules comprising the labeled nucleic acid.
75. A method for determining the presence of increased susceptibility to a glaucoma, to a progressive ocular hypertensive disorder resulting in loss of visual field, or the presence of steroid sensitivity in a patient, comprising the method of claim 74, wherein the sample containing DNA is derived from the patient.
76. The method of claim 75, which is performed during or after the patient is treated with a steroid compound.
77. The method of claim 75, which is performed prior to an administration of a steroid compound.
78. A kit for determining the presence of increased susceptibility to a glaucoma, to a progressive ocular hypertensive disorder resulting in loss of visual field, or the presence of steroid sensitivity in a patient, comprising a labeled nucleic acid of claim 70 and a means for detecting hybridization with the labeled nucleic acid.
79. A nucleic acid comprising a nucleotide sequence selected from the group consisting of one of SEQ ID NO: 1-3 or 34, and a fragment of SEQ ID NO: 1-3, or 34 that possesses a functional regulatory region.
80. A cell comprising an introduced nucleic acid of the sequence as claimed in claim 79.
81. A vector comprising a nucleic acid as claimed in claim 79.

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82. A method for detecting the specific binding of a molecule to a nucleic acid comprising providing a nucleic acid of claim 79, contacting the nucleic acid with a sample containing the molecule to be tested, and identifying binding of the molecule to the nucleic acid.
83. A method as claimed in claim 82, wherein the identifying step comprises a gel shift assay.
84. A method as claimed in claim 82, wherein the nucleic acid is labeled.
85. A method for detecting the presence of the TIGRmt11 sequence variation in a sample containing DNA, comprising providing amplification reaction primers that direct amplification of a selected nucleic acid region containing the T to C substitution of the TIGRmt11 sequence variant, amplifying the nucleic acid defined by the amplification reaction primers, and determining the presence or absence of the T to C substitution in the amplified nucleic acid.
86. The method of claim 85, wherein the determining the presence or absence of the T to C substitution comprises sequencing the amplified nucleic acid.
87. The method of claim 86, wherein the determining the presence or absence of the T to C substitution comprises a hybridization assay.
88. A method for determining the presence of increased susceptibility to a glaucoma, to a progressive ocular hypertensive disorder resulting in loss of visual field, or the presence of steroid sensitivity in a patient comprising the method of claim 85, wherein the sample containing DNA is derived from the patient.
89. A kit for determining the presence of increased susceptibility to a glaucoma, to a progressive ocular hypertensive disorder resulting in loss of visual field, or the presence of steroid sensitivity in a patient, comprising amplification reaction primers that direct amplification of a selected nucleic acid region containing the T to C substitution of the TIGRmt11 sequence variant and an enzyme for amplifying the region containing the T to C substitution.
90. A method for detecting a polymorphism in the 5' flanking region of a TIGR gene, comprising selecting amplification reaction primers from the group consisting of nucleic acids comprising nucleotide sequences SEQ ID NO: 6-25 or 35, or complements thereof, nucleotide sequences from a fragment of SEQ ID NO: 6-25 or 35, or their complements, and nucleotide sequences from an about 18 to an about 60 nucleotide fragment of the 5' flanking sequences in SEQ ID NO: 1-3, or 34, or complements thereof, amplifying a selected nucleic acid region of the 5' flanking region defined by the amplification reaction primers in a sample of DNA, and comparing at least part of the sequence of the amplified nucleic acid with the sequence set forth in SEQ ID NO: 1-3.

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